

Amendments to the Specification:

Please replace the paragraph beginning at page 3, line 31, with the following:

This invention provides an RNase A superfamily polypeptide having an N-terminus of the sequence: $X^1X^2SLX^3V$, wherein X^1 represents methionine or is absent, X^2 represents glycine or is absent, and X^3 represents an amino acid residue (SEQ ID NO:9), said RNase A superfamily polypeptide being selectively toxic to a proliferating endothelial cell.

Please replace the paragraph beginning at page 4, line 1, with the following:

In a preferred embodiment, the invention provides an RNase A superfamily polypeptide having the sequence of SEQ. ID. No. 2 SEQ ID NO:2. In another preferred embodiment, the invention provides an RNase A superfamily polypeptide having 90% homology to SEQ. ID. No. 2 SEQ ID NO:2. In yet another preferred embodiment, the invention provides an RNase A superfamily polypeptide having the sequence of SEQ. ID. No. 4 SEQ ID NO:4. In a further preferred embodiment, the invention provides an RNase A superfamily polypeptide having 90% homology to SEQ. ID. No. 4 SEQ ID NO:4. More preferably, the RNase A superfamily polypeptide has a N-terminus which is MGSLHV (SEQ ID NO:10). Most preferably, the invention provides an RNase A superfamily polypeptide wherein the N-terminus is MSLHV (SEQ ID NO:11), and the rest of the polypeptide includes the EDN amino acid sequence.

Please replace the paragraph beginning at page 4, line 17, with the following:

In yet another aspect, the invention provides a pharmaceutical composition comprising a unit dosage RNase A superfamily polypeptide comprising an N-terminus of the sequence: $X^1X^2SLX^3V$, wherein X^1 represents methionine or is absent, X^2 represents glycine or is absent, and X^3 represents an amino acid residue (SEQ ID NO:9), said RNase A superfamily

polypeptide being selectively toxic to a proliferating endothelial cell; and a pharmaceutically acceptable carrier.

Please replace the paragraph beginning at page 4, line 23, with the following:

In a further aspect, the invention provides a method of selectively inhibiting the growth of a proliferating endothelial cell by contacting said cell with an RNase A superfamily polypeptide comprising an N-terminus of the sequence: $X^1X^2SLX^3V$, wherein X^1 represents methionine or is absent, X^2 represents glycine or is absent and X^3 represents an amino acid residue (SEQ ID NO:9), said RNase A superfamily polypeptide being selectively toxic to a proliferating endothelial cell; and detecting the inhibition of the growth of said cell.

Please replace the paragraph beginning at page 5, line 1, with the following:

In one aspect, the invention provides a method of treating a patient with proliferating endothelial cells by administering an effective amount of an RNase A superfamily polypeptide comprising an N-terminus of the sequence: $X^1X^2SLX^3V$, wherein X^1 represents methionine or is absent, X^2 represents glycine or is absent, and X^3 represents an amino acid residue (SEQ ID NO:9), said RNase A superfamily polypeptide being selectively toxic to a proliferating endothelial cell; and detecting the amelioration of Kaposi sarcoma in said patient.

Please replace the paragraph beginning at page 5, line 20, with the following:

Figure 1 shows a sequence alignment of some members of the RNase A superfamily: Frog lectin is from Rana catesbeiana (Rana catesbeiana (SEQ ID NO:18)), onconase (SEQ ID NO:19), EDN (SEQ ID NO:6), ECP (human eosinophil cationic protein) (SEQ ID NO:20), ANG is bovine angiogenin (SEQ ID NO:21), seminal is bovine seminal RNase (SEQ ID NO:22), and RNase A is bovine pancreatic RNase A (SEQ ID NO:23). Amino acids

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conserved in all members are capitalized, and active site residues H12, K41, and H119 (RNase A numbering) are marked with an asterisk.

Please replace the paragraph beginning at page 5, line 26, with the following:

Figure 2 shows the comparison of the sequences of the N-termini of rEDN (SEQ ID NO:24) and (-4)rEDN (SEQ ID NO:25).

Please replace the paragraph beginning at page 6, line 26, with the following:

Figure 8 shows a map of the (-4)rhEDN-g3p fusion construct. A DNA fragment encoding (-4)rhEDN was cloned into the phagemid vector pCANTAB5E (Pharmacia). The pCANTAB5E vector is comprised of a leader sequence (SS), followed by the peptide SLHV (SEQ ID NO:16) which is fused to the EDN coding region. The sequence denoted TAG is an amber stop codon. The sequence GGGGS (SEQ ID NO:17) is a peptide sequence which was inserted to allow more flexibility for the folding of (-4)rhEDN. The sequence g3p refers to the g3p coding sequence.

Please replace the paragraph beginning at page 14, line 3, with the following:

The modified RNase A superfamily polypeptides can be manufactured by adding to the N terminus of mature EDN protein a short amino acid sequence in the length of 4-6 amino acids. The N-terminus has the sequence: X¹X²SLX³V, wherein X¹ represents methionine or is absent, X² represents glycine or is absent, and X³ represents an amino acid residue (SEQ ID NO:9). For example, the N terminus can have the sequence of MGSLXV (SEQ ID NO:12), MSLXV (SEQ ID NO:13), GSLXV (SEQ ID NO:14), or SLXV (SEQ ID NO:15), where X is an amino acid.

Please replace the paragraph beginning at page 20, line 6, with the following:

The polypeptides of the present invention are cytotoxic against the Lewis lung cell line, which is a model for angiogenesis. The Lewis lung cell line is a mouse lung carcinoma cell line. ~~(YES/NO?)~~ They are deposited with ATCC, under the Accession No. CRL-1642. ~~(YES/NO?)~~

Please replace the paragraph beginning at page 28, line 2, with the following:

A 5' oligonucleotide was designed to incorporate amino acids, SLHV (SEQ ID NO:16), to be located in positions -4 to -1 of the first amino acid of EDN. The format of the 5' primer oligonucleotide is as follows:

5' - ATATA-**TCTAGA**-*AATAATTTGTTAACTTAAGAAGGAGATA***CAT-ATG-**
TCACTCCATGTC-*AAACCGCCGCAGTC*ACTTGG - 3' ~~SEQ ID No.: 7~~ SEQ ID NO:7
where the first 5 base pairs (bp) provide a clamp for the restriction enzyme, the bold sequence is an XbaI restriction site, the italicized sequence is a modified vector sequence, the underlined ATG is the initiating methionine sequence, the underlined bold sequence codes for SLHV (SEQ ID NO:16) amino acids and the underlined italicized sequence is the first 7 amino acids of EDN.

Please replace the paragraph beginning at page 28, line 14, with the following:

The 3' primer oligonucleotide is as follows and given in the 5' to 3' orientation:
5' - GTTCATCTGGACCGTATCATC-*TAGTAG-GGATCC-GCGCG* - 3' ~~SEQ ID No.: 8~~
SEQ ID NO:8

where the first 21 bps code for the last 7 amino acids of EDN, the italicized sequence codes for 2 stop signals, the bold italicized sequence is the BamHI restriction site and the bold sequence provides a clamp for the restriction enzyme.

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Please replace the paragraph beginning at page 34, line 8, with the following:

A DNA fragment encoding (-4)rhEDN was cloned into the phagemid vector pCANTAB5E (Pharmacia). This vector permits the expression of genes cloned into it as a g3p fusion protein. The pCANTAB5E vector is comprised of a leader sequence (SS) that directs secretion of the g3p fusion protein to the surface of the bacteria. See Fig. 8. The E tag consists of a 21 amino acid peptide to which a commercial antibody is available for detecting expression. The sequence denoted TAG is an amber stop codon. See Fig. 8. The TAG in the commercial vector was changed from its position behind the Etag to a new position behind the signal peptide EDN for release of the protein during certain expression systems. A GGGGS (SEQ ID NO:17) peptide sequence was inserted between the (-4)rhEDN and the g3p protein to allow more flexibility of folding the (-4)rhEDN. The four amino acids attached to the amino terminus of rhEDN are SLHV (SEQ ID NO:16).

Please insert the accompanying paper copy of the Sequence Listing, page numbers 1 to 12, at the end of the application.